APPLICANTS: Baker et al. SERIAL NO: 10/701,265

DOCKET NO: ISIS-5300

AMENDMENTS TO THE CLAIMS: This listing of claims replaces all prior versions and listings of claims in the instant patent application.

What Is Claimed Is:

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1-119. (canceled)

120. (new) A composition comprising a duplex consisting of a first chemically synthesized oligomeric compound and a second chemically synthesized oligomeric compound, wherein:

each of the first chemically synthesized oligomeric compound and the second chemically synthesized oligomeric compound independently consists of 17 to 25 linked nucleosides, each nucleoside comprising a nucleobase and a sugar;

at least 17 contiguous nucleobases of the first chemically synthesized oligomeric compound are 100% complementary to at least 17 contiguous nucleobases of the second chemically synthesized oligomeric compound;

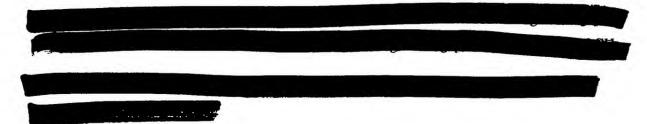
the first chemically synthesized oligomeric compound and the second chemically synthesized oligomeric compound are not covalently linked to each other; and

the first chemically synthesized oligomeric compound is a gapmer, wherein the gap comprises at least 4 nucleosides, each comprising a 2'-OH, and wherein each nucleoside of each wing comprises a 2' modification or is an LNA nucleoside.

- (new) The composition of claim 120, wherein the second chemically synthesized oligomeric compound is a gapmer, wherein the gap comprises at least 4 nucleosides, each comprising a 2'-OH, and wherein each nucleoside of each wing comprises a 2' modification or is an LNA nucleoside.
- 122. (new) The composition of claim 120, wherein the duplex comprises an overhang on the 5' end, on the 3' end, or on both the 5' end and the 3' end.
- 123. (new) The compound of claim 120, wherein the duplex is blunt-ended.

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124. (new) The composition of claim 120, wherein each nucleoside of at least one of the wings of the gapmer comprises a 2' sugar modification selected from fluor, alkoxy, amino-alkoxy, allyloxy, imidazolylalkoxy, and methoxyethoxy or is an LNA nucleoside.



127. (new) The composition of claim 120, wherein each nucleoside of the 3' wing of the gapmer comprises a 2'- OCH₃.

er comprises a 2'- OCH₃.

- npound is a sea extrand.
- (new) The composite of claim 128, wherein that chemically synthesized oligome compound is an antisense strand.
- (new) The composition of claim erein each nucleoside of one wing of the gapm prises a 2'-fluoro and each nucleoside of the other wing of the gapmer is an LNA.
- (new) The composition of claim 120, wherein each nucleoside of the 3' wing of the gener is an LNA.
- (new) The omposition of claim 126, wherein each nucleoside of the Saving of the mer is LNA.
- (new) The composition of claim 133, wherein the first chemically synthesized oligation

136. (new) The composition of claim 120, wherein each wing of the gapmer is from two to seven nucleosides in length.

- 137. (new) The composition of claim 120, wherein at least one of the first chemically synthesized oligomeric compound and the second chemically synthesized oligomeric compound comprises at least one phosphorothioate linkage.
- 138. (new) The composition of claim 137, wherein each of the first chemically synthesized oligomeric compound and the second chemically synthesized oligomeric compound comprises at least one phosphorothioate linkage.
- 139. (new) A compound comprising a chemically synthesized oligomeric compound, wherein:

 the chemically synthesized oligomeric compound consists of 17 to 25 linked nucleosides,
 each nucleoside comprising a nucleobase and a sugar;

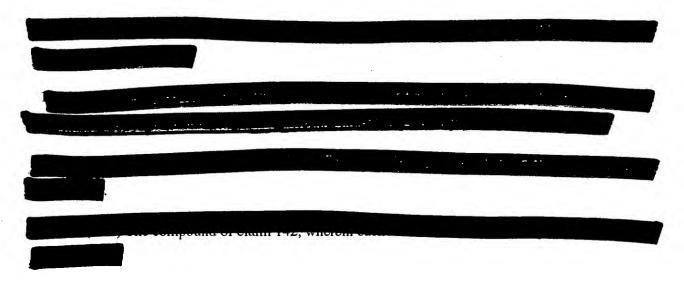
the chemically synthesized oligomeric compound is a gapmer, wherein the gap comprises at least 4 nucleosides, each comprising a 2'-OH, and wherein each nucleoside of each wing comprises a 2' modification or is an LNA nucleoside; and

the chemically synthesized oligomeric compound is an antisense compound.

140. (new) The compound of claim 139, wherein each nucleoside of at least one of the wings of the gapmer comprises a 2' sugar modification selected from fluoro, alkoxy, amino-alkoxy, allyloxy, imidazolylalkoxy, and methoxyethoxy or is an LNA nucleoside.

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143. (new) The compound of claim 139, wherein each nucleoside of the 3' wing of the gapmer comprises a 2'- OCH₃.



- 148. (new) The compound of claim 139, wherein each wing of the gapmer is from two to seven nucleosides in length.
- 149. (new) The compound of claim 139, wherein the chemically synthesized oligomeric compound comprises at least one phosphorothioate linkage.

